

Positive 52-Week Maintenance Data Observed with Rademikibart in Patients with Moderate-to-Severe Atopic Dermatitis (SEAS/DE CHINA)

Jianzhong Zhang,¹ Jonathan I. Silverberg,² Jiawang Guo,³ Jili Yun,³ Wuban Pan,³ Zheng Wei,⁴ Raúl Collazo⁴

¹Peking University People's Hospital, Department of Dermatology, Beijing, China; ²Department of Dermatology, George Washington University School of Medicine and Health Sciences, Washington, DC, USA; ³Suzhou Connect Biopharmaceuticals Ltd, Taicang, China; ⁴Connect Biopharma LLC, San Diego, CA, USA

Disclosures for Prof. Jianzhong Zhang

- Connect Biopharma – Clinical Trial Investigator

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Rademikibart

Rademikibart is a next-generation mAb, optimized for high affinity binding to the IL-4R α subunit, potentially allowing **convenient monthly dosing** intervals.^{1,2}

SEAS/DE CHINA

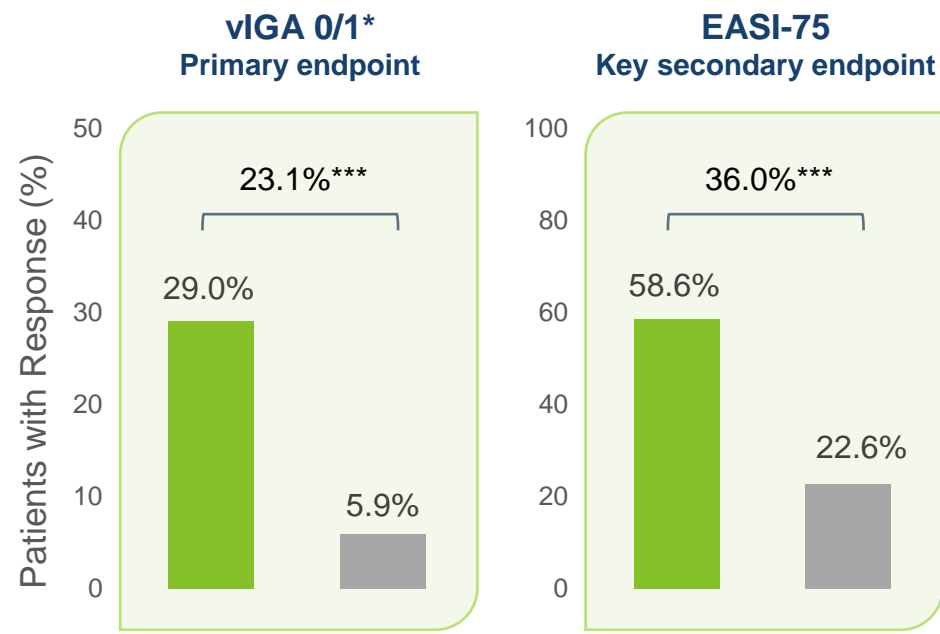
In **Stage 1** of SEAS/DE CHINA (CN-002), patients with moderate-to-severe AD, all primary and secondary endpoints (e.g. vIGA 0/1, EASI, PP-NRS) were achieved at Week 16 with Q2W dosing

Stage 2 assessments were conducted across an additional 36 weeks following re-randomization with either Q2W or Q4W dosing

Objective

To report efficacy and safety from **Stage 2** across 52 weeks in SEAS/DE CHINA.

Week 16 in SEAS/DE CHINA^{3,†}



*vIGA 0/1 and ≥ 2 -point reduction.

†N=330 (N=255 in reference 3).

***P<0.001 vs placebo.

■ Rademikibart Q2W (n=219)

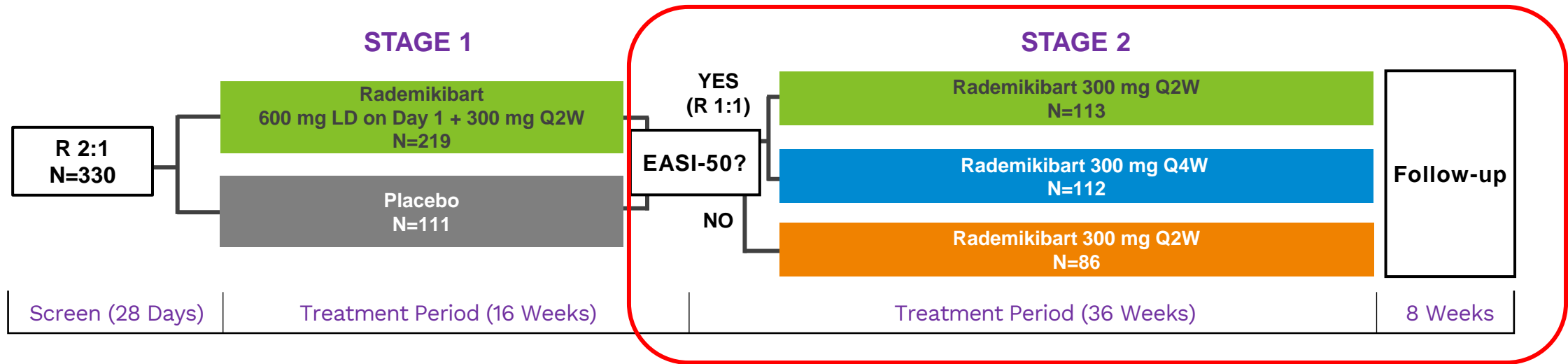
■ Placebo (n=111)

References: 1. Zhang L, et al. Sci Rep. 2023;13:12411. 2. Silverberg JI, et al. J Allergy Clin Immunol. 2024;153:1040-1049.e12. 3. Zhang J, et al. Oral presentation #45874, AAD 2023, New Orleans, LA, USA.

Abbreviations: AD = atopic dermatitis. EASI = Eczema Area and Severity Index. EASI-75 = at least 75% decrease from baseline. IL, interleukin. IL-4R α = IL-4-receptor alpha. mAb = monoclonal antibody. PP-NRS = Peak Pruritus Numeric Rating Scale. Q2W = every 2 weeks. Q4W = every 4 weeks. vIGA 0/1 = validated Investigator Global Assessment of 0 (clear skin) or 1 (almost clear).

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Study Design, Inclusion Criteria, Endpoints, and Treatment Completion Rates



Key inclusion criteria:

- 12–75 years of age
- Atopic dermatitis for ≥ 1 year
- EASI ≥ 16
- vIGA ≥ 3 (5-point scale [0-4])
- $\geq 10\%$ BSA involvement
- PP-NRS ≥ 4

Week 16 EASI-50 responders were re-randomized 1:1 to rademikibart 300 mg Q2W or Q4W

Primary endpoint:

- vIGA 0/1 (including ≥ 2 -point reduction) response at Week 16

Other efficacy endpoints included:

- EASI-75 and EASI-90 response at Week 16
- PP-NRS ≥ 3 - and ≥ 4 -point response at Week 16
- % changes from baseline in EASI and PP-NRS scores at Week 16
- These efficacy outcomes during the 36-week treatment period

Patients completing treatment:

At Week 16

- 94.2% (rademikibart Q2W or placebo)

At Week 52

- 92.4% of Week 16 EASI-50 responders (Q2W or Q4W)
- 89.5% of Week 16 EASI-50 non-responders (Q2W)

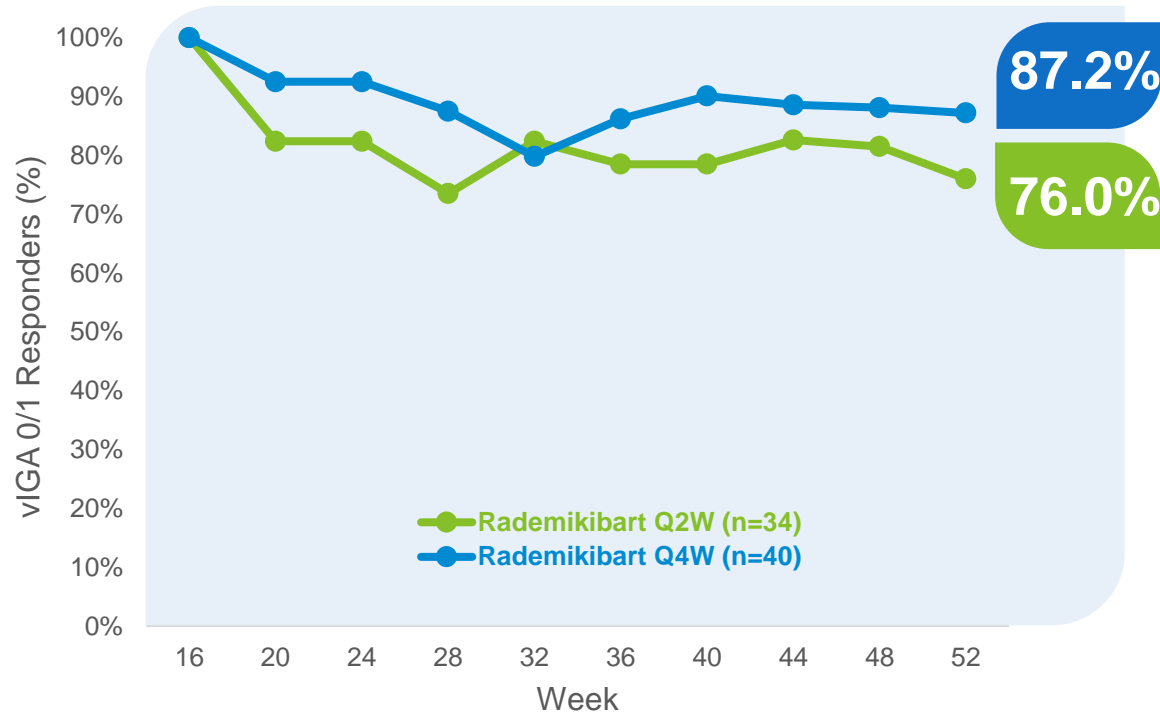
To maintain blinded state, all patients received placebo between Q4W doses of rademikibart 300 mg.

Abbreviations: BSA = Body Surface Area. EASI = Eczema Area and Severity Index. EASI-50, EASI-75, and EASI-90 = at least 50%, 75%, and 90% decrease from baseline. LD = Loading Dose. PP-NRS = Peak Pruritus Numeric Rating Scale. Q2W = every 2 weeks. Q4W = every 4 weeks. R = randomized. vIGA 0/1 = validated Investigator Global Assessment of 0 (clear skin) or 1 (almost clear).

Maintenance of IGA 0/1 and EASI-75 Responses Observed at Week 16 were Sustained Through Week 52

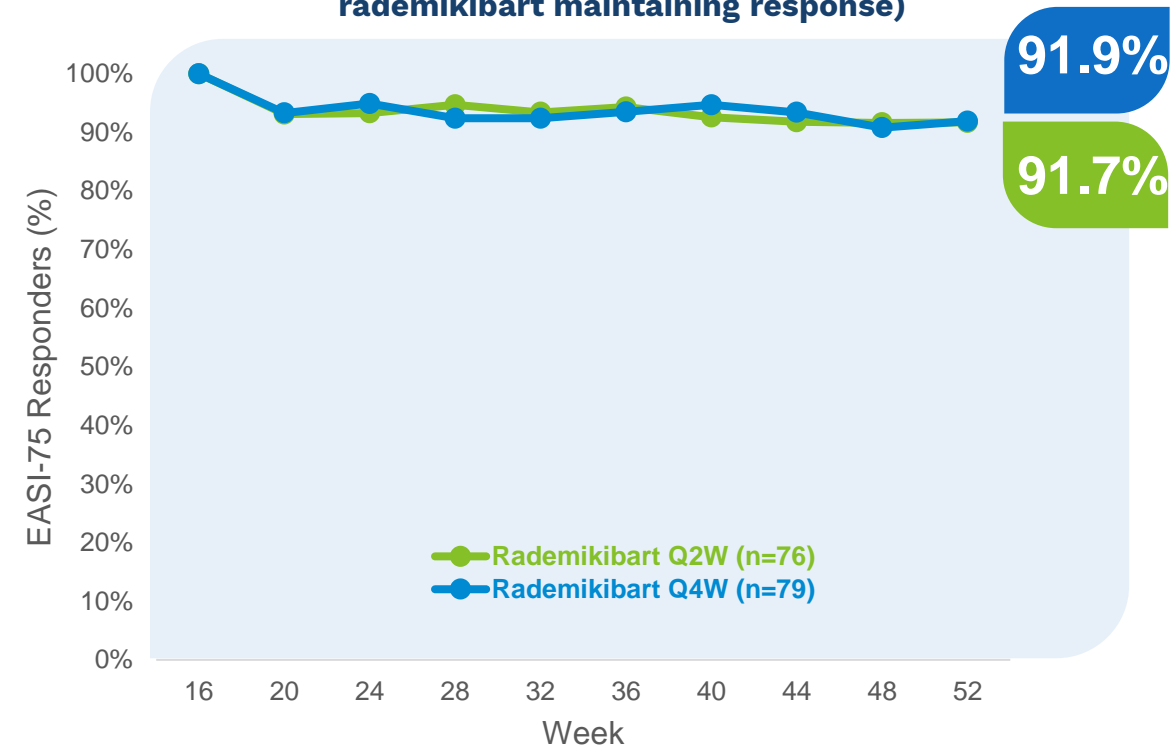
vIGA 0/1 and ≥2-Point Reduction

(Percentage of Week 16 vIGA 0/1 responders to rademikibart maintaining response)*



EASI-75

(Percentage of Week 16 EASI-75 responders to rademikibart maintaining response)



*Patients with both EASI-50 and IGA 0/1 responses at Week 16

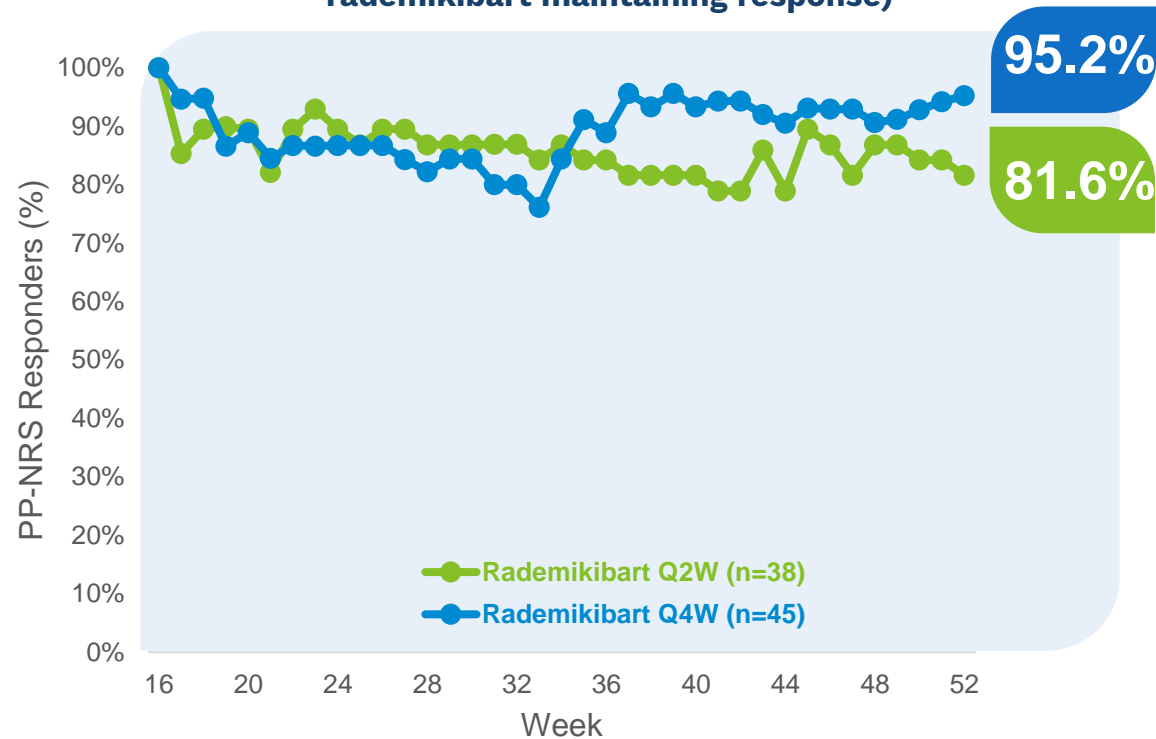
Q2W = Continued on Q2W dosing from Week 16. Q4W = Switched from Q2W to Q4W dosing at Week 16.

Data were analyzed by NRI-MI (non-responder imputation for rescue medications and multiple imputation for remaining missing data).

Abbreviations: EASI = Eczema Area and Severity Index. EASI-50 = at least 50% decrease from baseline. Q2W = every 2 weeks. Q4W = every 4 weeks. vIGA 0/1 = validated Investigator Global Assessment of 0 (clear skin) or 1 (almost clear).

PP-NRS ≥ 4 -Point Responses were also Highly Maintained from Week 16 Through Week 52

PP-NRS ≥ 4 -Point Reduction (Percentage of Week 16 PP-NRS responders to rademikibart maintaining response)*



*Patients with both EASI-50 and PP-NRS responses at Week 16

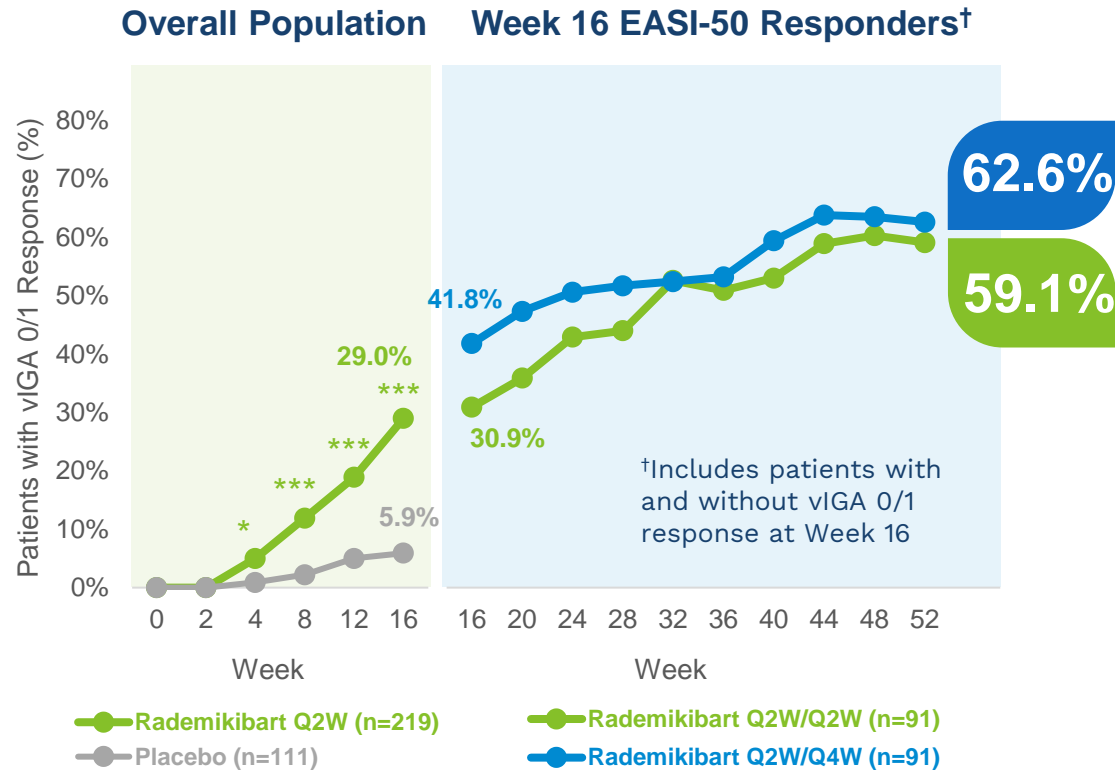
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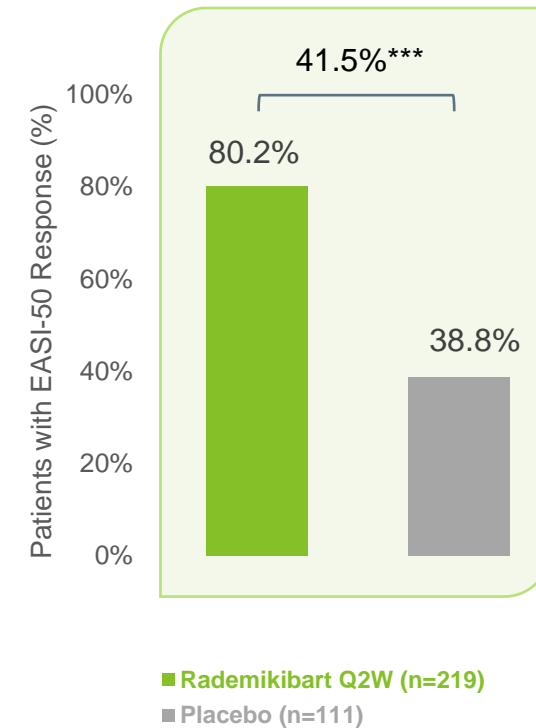
Abbreviations: EASI = Eczema Area and Severity Index. EASI-50 = at least 50% decrease from baseline. PP-NRS = Peak Pruritus Numerical Rating Scale. Q2W = every 2 weeks. Q4W = every 4 weeks.

Among EASI-50 Responders, Continued Improvement of IGA 0/1 Response was Observed with Rademikibart (through Week 52)

vIGA 0/1 and ≥2-point reduction



EASI-50 Response at Week 16

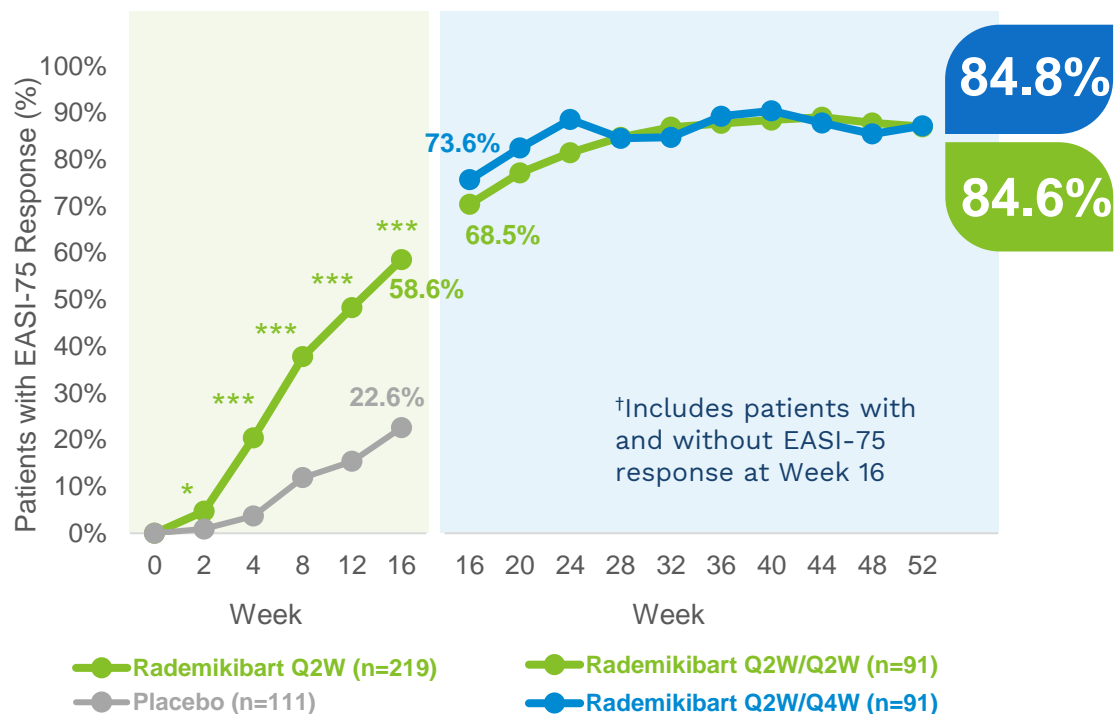


Q2W/Q2W = Continued on Q2W dosing from Week 16. Q2W/Q4W = Switched from Q2W to Q4W dosing at Week 16. ***, **, * for P<0.001, <0.01, <0.05, respectively, vs placebo. Missing data in the rademikibart group up to Week 16 was imputed by jump to reference imputation (J2R) after applying the rule of intercurrent events; multiple imputation was used for the placebo arm. From Week 16, binary response data were analyzed by non-responder imputation and multiple imputation. **Abbreviations:** EASI = Eczema Area and Severity Index. EASI-50 = at least 50% decrease from baseline. Q2W = every 2 weeks. Q4W = every 4 weeks. vIGA 0/1 = validated Investigator Global Assessment of 0 (clear skin) or 1 (almost clear).

Continued Improvement of EASI-75 and PP-NRS were Observed with Rademikibart Treatment (Baseline through Week 52)

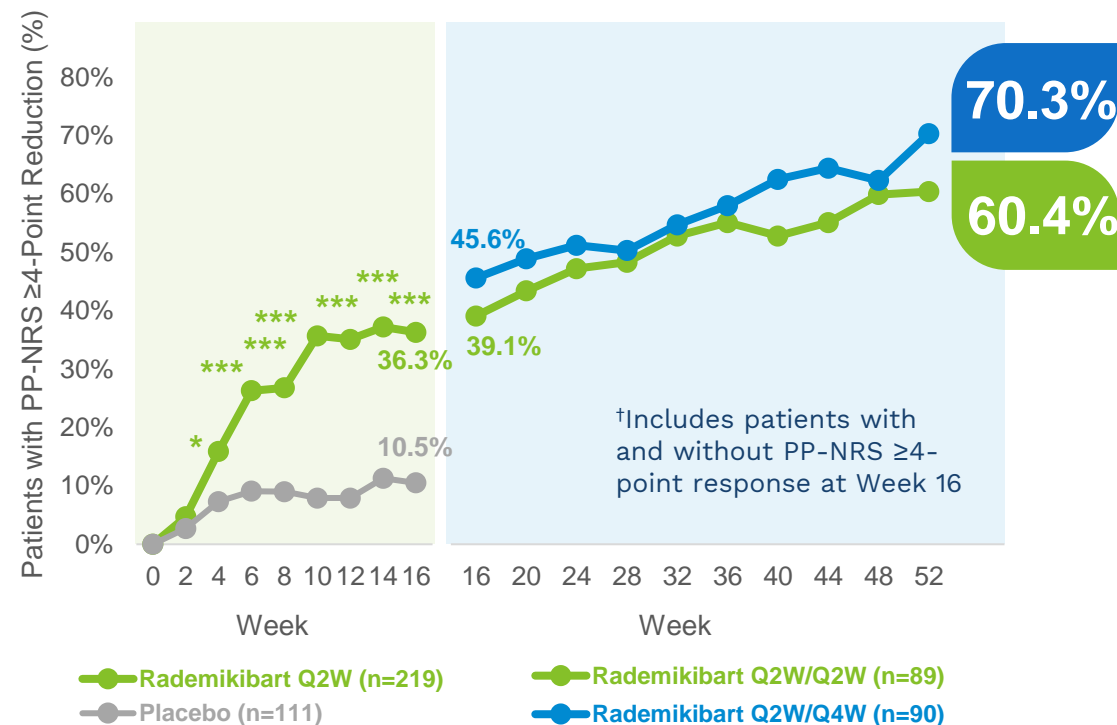
EASI-75

Overall Population Week 16 EASI-50 Responders[†]



PP-NRS ≥4-Point Reduction

Overall Population Week 16 EASI-50 Responders[†]

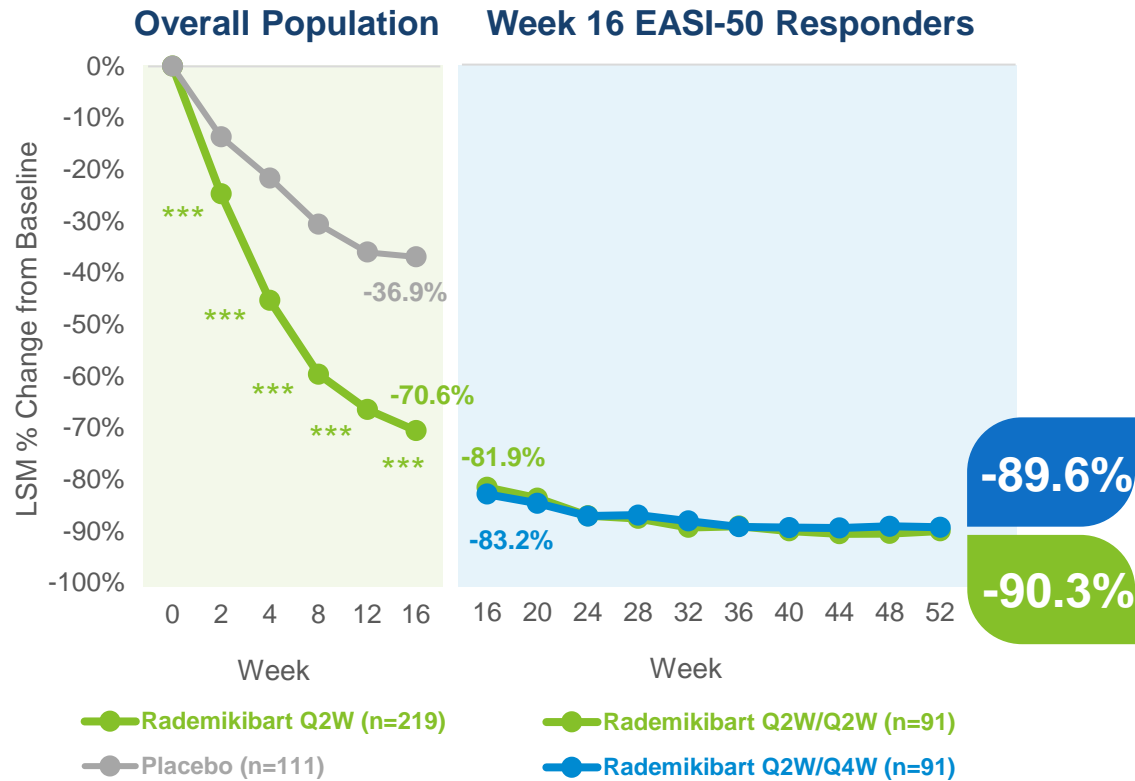


Q2W/Q2W = Continued on Q2W dosing from Week 16. Q2W/Q4W = Switched from Q2W to Q4W dosing at Week 16. ***, **, * for P<0.001, <0.01, <0.05, respectively, vs placebo.

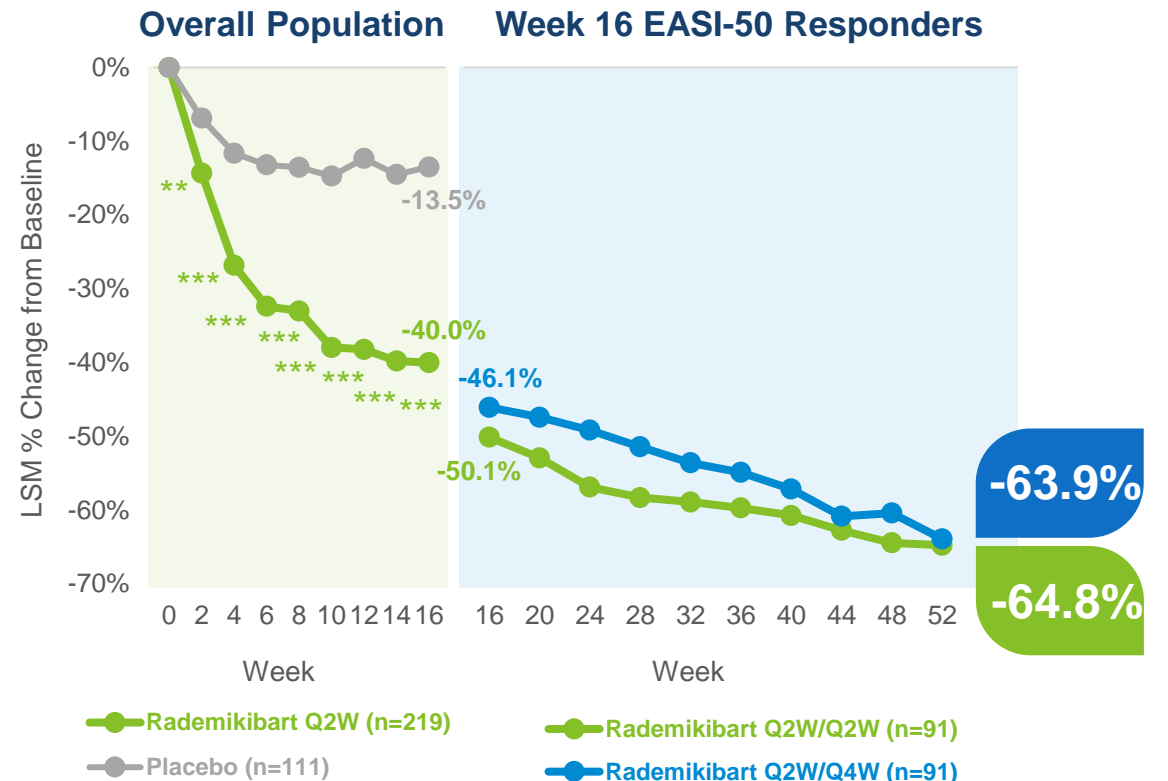
Missing data in rademikibart group up to Week 16 was imputed by jump to reference imputation (J2R) after applying the rule of intercurrent event; multiple imputation was used for the placebo arm. From Week 16, binary response data were analyzed by non-responder imputation and multiple imputation. **Abbreviations:** EASI = Eczema Area and Severity Index. EASI-75/90 = at least 75/90% decrease from baseline. Q2W = every 2 weeks. Q4W = every 4 weeks.

Continued Improvement of EASI and PP-NRS Scores were Observed with Rademikibart (Baseline through Week 52)

EASI Score



PP-NRS Score



Q2W/Q2W = Continued on Q2W dosing from Week 16. Q2W/Q4W = Switched from Q2W to Q4W dosing at Week 16. ***, **, * for P<0.001, <0.01, <0.05, respectively, vs placebo. Missing data in the rademikibart group up to Week 16 was imputed by jump to reference imputation (J2R) after applying the rule of intercurrent event; multiple imputation was used for the placebo arm. From Week 16, score change data were analyzed by ANCOVA and multiple imputation. **Abbreviations:** ANCOVA = Analysis of Covariance. EASI = Eczema Area and Severity Index. EASI-50 = at least 50% decrease from baseline. LSM, least squares mean. PP-NRS = Peak Pruritus Numerical Rating Scale. Q2W = every 2 weeks. Q4W = every 4 weeks.

No new safety signals compared with previous rademikibart trials,^{1,2} including no treatment-related serious events

n (%) patients with...	Stage 1 (Weeks 0–16)		Stage 2 (Weeks 16–60)		
	Rademikibart Q2W N=219	Placebo N=111	Rademikibart Q2W (W16 responders)* N=113	Rademikibart Q4W (W16 responders)* N=112	Rademikibart Q2W, (W16 non-responders)* N=85
Any TEAE	166 (75.8%)	80 (72.1%)	93 (82.3%)	95 (84.8%)	71 (83.5%)
Serious TEAEs – none were related to study treatment and no deaths	1 (0.5%)	3 (2.7%)	1 (0.9%)	3 (2.7%)	6 (7.1%)
Severe (Grade 3) TEAEs	4 (1.8%)	5 (4.5%)	3 (2.7%)	5 (4.5%)	6 (7.1%)
TEAEs leading to treatment discontinuation [†]	2 (0.9%)	1 (0.9%)	0	0	1 (1.2%)
Injection site reaction – all mild (Grade 1)	20 (9.1%)	3 (2.7%)	6 (5.3%)	8 (7.1%)	6 (7.1%)
Conjunctivitis [‡]	12 (5.5%)	3 (2.7%)	6 (5.3%)	6 (5.4%)	7 (8.2%)
Herpes infection [#]	4 (1.8%)	2 (1.8%)	0	0	3 (3.5%)

*Week 16 EASI-50 responders or non-responders.

[†]Discontinuations were due to atopic dermatitis flare in the rademikibart Q2W (Grade 2) and placebo (Grade 3) during Stage 1, pregnancy (classified as a TEAE) in Stage 2, and vitiligo (Grade 2) that developed in Stage 1 (rademikibart 300 mg Q2W arm) and discontinuation occurred in Stage 2.

[‡]Conjunctivitis includes the preferred terms conjunctivitis, allergic conjunctivitis, conjunctival injection, bacterial conjunctivitis, viral conjunctivitis, giant papillary conjunctivitis, eye irritation, and eye inflammation.

[#]Herpes infections includes the preferred terms herpes virus infection, herpes zoster, herpes simplex, herpes simplex reactivation, oral herpes.

References: 1. Wang J, et al. Clin Transl Sci. 2023;16:2614-2627. 2. Silverberg JI, et al. J Allergy Clin Immunol. 2024;153:1040-1049.e12.

Abbreviations: EASI = Eczema Area and Severity Index. EASI-50 = at least 50% decrease from baseline. Q2W = every 2 weeks. Q4W = every 4 weeks. TEAE = treatment-emergent adverse event.

Conclusion:

SEAS/DE CHINA supports long-term monthly dosing of rademikibart

Efficacy continuously improved through Week 52

- Skin clearance (IGA0/1, EASI) and pruritus (PP-NRS) improvements at Week 16 in SEAS/DE CHINA (dosed Q2W) were compatible with WW001 global Phase 2 trial results (dosed Q2W and Q4W).¹
- Efficacy continued to improve between Weeks 16 and 52 and was comparable with rademikibart Q2W and Q4W.

Binary responses at Week 16 were highly maintained through Week 52

- Most patients with response at Week 16 maintained them through Week 52.
- Maintenance rates were comparable with rademikibart Q2W and Q4W: IGA0/1 (76.0%, 87.2%), EASI-75 (91.7%, 91.9%), PP-NRS \geq 4-point reduction (81.6%, 95.2%).
- Maintenance rates were higher than reported for approved AD biologic therapies (dupilumab and tralokinumab).^{2,3}

Well tolerated through Week 52

- No new safety signals.
- Few TEAEs led to discontinuation.
- No serious TEAEs were related to study treatment.

References: 1. Silverberg JI, et al. J Allergy Clin Immunol. 2024;153:1040-1049.e12. 2. Wollenberg A, et al. Br J Dermatol. 2021;184:437-449. 3. Worm M, et al. JAMA Dermatol. 2020;156:131-143.

Abbreviations: EASI = Eczema Area and Severity Index. EASI-75 = at least 75% decrease from baseline. PP-NRS = Peak Pruritus Numeric Rating Scale. Q2W = every 2 weeks. Q4W = every 4 weeks. TEAE = treatment-emergent adverse event. vIGA 0/1 = validated Investigator Global Assessment of 0 (clear skin) or 1 (almost clear) and \geq 2-point reduction.